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of rugose is recessive to the sterility of both glazed and wax. In the glazed-wax hybrid a similar relation holds for the somatic effect, glazed being dominant to wax. The high degree of sterility in both homozygous parent forms here, however, would naturally call for the observed sterility of the hybrid and eliminates the question of dominance with respect to this feature.

From the above standpoint sterility in the rugose-glazed and rugose wax hybrids is accounted for by assuming the dominance of sterility instead of assuming an incompatibility as was done in the previous paper when only the rugose-glazed hybrids were known. The present explanation calls for the occasional occurrence of fertile hybrids between rugose and glazed to correspond to the occasional fertility in pure glazed females. No such fertile hybrids have been obtained thus far, but this may be due merely to chance, since only a very few of them would be expected in the number of females tested. This conclusion is made still more probable by the occurrence of the one fertile hybrid between rugose and wax.

[1] These PROCEEDINGS, **3,** 1917 (673).

[2] These three characters are almost certainly allelomorphs, although the sterility of the hybrids and the dominance of the normal somatic constitution of rugose females makes it difficult to demonstrate the fact for the latter character. See Metz, C. W., *Genetics,* **3,** 1918 (116).

[3] The females were tested both singly and in mass cultures. The use of some mass cultures prevents recording the exact number of flies actually tested, for in these a few females may have died before they had a chance to breed.

[4] In each case these are such as to indicate fertility, not contamination or non-disjunction. In one case both parents were glazed, the offspring being 3 glazed females and 5 glazed males.

[5] It is difficult to obtain accurate determinations of the relative degrees of fertility of the males in these cases, for even the wax males breed fairly well, but in general the relations seem to be as described.

[6] Since the characters are sex linked and apparently allelomorphic no truly "hybrid" males can be obtained.

[7] In this and the preceding experiment offspring were obtained from two or three other bottles, but they were such as to indicate that they probably came from females heterozygous for one factor only, due to non-virginity or contamination.

STUDIES ON THE TRANSFORMATION OF THE INTESTINAL FLORA, WITH SPECIAL REFERENCE TO THE IMPLANTATION OF BACILLUS ACIDOPHILUS. I. FEEDING EXPERIMENTS WITH ALBINO RATS

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Communicated by L. B. Mendel, May 28, 1920

The type of bacteria developing in the alimentary tract may be influenced in a noteworthy manner, not only through special alterations in the chemical composition of the diet, but also through the ingestion of living cultures of *Bacillus acidophilus* (Moro) with or without accompanying carbohydrates.

When added in sufficient amounts to the basal diet of bread and meat, namely 2 grams daily, lactose and dextrin caused a very pronounced transformation of the intestinal flora of white rats within three to six days, and stimulated the development of *B. acidophilus* to such an extent that it entirely dominated the flora, thus suppressing or displacing almost completely all other bacterial types commonly found in the enteric tract. The simple flora persisted as long as the feeding of these carbohydrates was continued. *B. bifidus* (Tissier) occasionally increased in numbers under these dietary conditions, but as a rule it remained relatively obscure.

Maltose, saccharose and glucose exercised no transforming influence on the types of bacteria present. These results are in perfect agreement with those of Distaso and Schiller (1914) and Hull and Rettger (1917). Torrey (1919) claims, however, to have obtained a moderate increase in the numbers of *B. acidophilus* as a result of sucrose feeding in dogs.

The most plausible explanation of the favorable influence of lactose and dextrin feeding on the implantation of *B. acidophilus* is one which rests to a large extent upon the fact that in the rat at least they are not completely absorbed before they reach the large intestine. Here they establish an optimum environment by serving as a readily available source of energy for *B. acidophilus.* This theory was advanced by Hull and Rettger who found a direct relationship between the rapid development of *B. acidophilus* and the presence of a reducing substance in the contents of the colon and rectum after lactose feeding. These findings have been confirmed in the present investigation, not only in connection with the administration of lactose but also dextrin. No reducing substances could be detected, however, after the feeding of maltose, sucrose or glucose.

The stimulating influence of lactose and dextrin on the development of aciduric organisms in the intestine does not depend upon increased acidity of the intestinal contents, as hydrogen ion concentration determinations made on the fecal material of the caecum and colon of rats receiving these carbohydrates showed. The hydrogen ion concentration limits remained essentially the same during the preliminary and the transforming periods of the different experiments.

The feeding of 1 gram of lactose or dextrin daily to white rats brought about a partial transformation which never amounted to more than 50% of the entire flora. These results are in harmony with the findings of Hull and Rettger (1917) who likewise demonstrated that 2 grams of lactose are necessary to cause a complete transformation. They showed further that larger amounts than 2 grams of lactose stimulate *B. bifidus* to increased activity, and that when as much as 3 grams of lactose is administered daily the Tissier organism assumes the chief rôle, thus supplanting *B. acidophilus* even.

The addition of 1 cc. of *B. acidophilus* suspension (McFarland nephelometer turbidity scale of 5) to 1 gram of lactose or dextrin brought the *B. acidophilus* level to the same point as when 2 grams of either lactose or dextrin were fed. The simplification of flora was rapid and complete, and *B. acidophilus* persisted as the dominating type as long as the combined feeding of *B. acidophilus* and the carbohydrate continued. Furthermore, the administration of 2 cc. daily of the *B. acidophilus* culture or suspension without the carbohydrates results in the intestinal implantation of *B. acidophilus* and the complete suppression of the other bacterial types which are ordinarily present in the enteric tract of the white rat. The response of the different rats to the pure culture feeding was practically the same in all of the subjects. It was of special interest to note, further, that the various curves which represent the development of *B. acidophilus* in the feces of the rats were of practically the same height and character, whether 2 grams of lactose or dextrin, or 1 gram of either of these carbohydrates together with 1 cc. of the *B. acidophilus* culture, or 2 cc. of the culture alone were fed daily.

Post-mortem examination of the different sections of the alimentary canal of rats harboring the simplified flora in the lower intestine revealed a general distribution of *B. acidophilus* throughout the length of the intestine.

Since the bacteria within the digestive tract procure their pabulum directly or indirectly from the diet consumed by the host, it is but logical to assume that there must be a definite relationship between the chemical nature of the ingested food and the metabolic activities of the intestinal organisms. Many investigators have noted that marked changes in the intestinal flora follow sharp alterations in the diet, especially from a high protein to a high caloric diet and vice versa. However, the so-called "high calory diets" can at best accomplish a short-lived bacterial reformation only, that is a change in metabolic activities of organisms already present from the putrefactive to the fermentative type. This shifting of bacterial metabolism is not necessarily accompanied by an elimination of undesirable bacteria from the alimentary tract. Lactose and dextrin, among the carbohydrates studied, alone have the property of stimulating the development of aciduric organisms.

Repeated attempts in the present investigation to establish *B. bulgaricus* in the alimentary canal of albino rats through the administration of extremely large numbers (5 cc. of suspensions) of this organism were entirely unsuccessful. At no time was *B. bulgaricus* recovered from the feces or from any portion of the digestive tract, whether the organism was fed alone or together with a utilizable carbohydrate. The contention of Metchnikoff and his followers that *B. bulgaricus* lends itself readily to implantation in the digestive tract of man receives no support whatever from the present observations upon white rats.

Although considerable doubt must be cast upon Metchnikoff's explanation of the merits of the sour-milk therapy, we may be compelled to accept the fundamental principle of his arguments. That is, bacterial implantation with the concomitant transformation of the intestinal flora, is without doubt, both desirable and possible, but it is possible only when living cultures of properly qualified organisms are employed, or when such specific diets are administered which will stimulate and favor such a transformation. *B. bulgaricus* is not of intestinal origin and is incapable of accommodating itself to intestinal conditions. *B. acidophilus*, on the other hand, is of intestinal origin and has shown itself to submit readily to implantation in the intestine of the white rat at least.

In many of the experiments of Metchnikoff and his pupils large quantities of milk were consumed as milk cultures of *B. bulgaricus*. Hull and Rettger showed that milk, when given in sufficient amounts to rats causes a rapid development of *B. acidophilus* in the intestine which may result in the complete suppression of other forms of bacteria. These observations were confirmed in the present investigations, not only for rats but also in numerous milk-feeding experiments on man. Milk owes this property to the lactose. It is not at all unlikely that what Metchnikoff and his pupils regarded as *B. bulgaricus* in the feces of animals and of human subjects was in reality *B. acidophilus*. These two organisms resemble each other so closely that one may easily be mistaken for the other. The above assumption is strengthened further by the statement of Belonowsky (1907) that the intestinal flora of nursing mice was of the same character as that of the older mice receiving the *B. bulgaricus* (milk) culture.

The feeding of *B. bulgaricus* without due regard to the use of milk can have little or no importance attached to it. The beneficial results which have been attributed to yogurt and other oriental sour-milk products have in all probability been due to the milk as such, rather than to the acid-producing bacteria contained in these products.

For a full account of the present investigation the reader is referred to the doctorate thesis of Harry A. Cheplin in the Yale University Library. The methods and results of these experiments, together with those conducted on man, will be published at an early date in unabridged form.